

REMARKS

Claims 12-34, 38-53, 56-62, 64, 66, 68 and 70-77 are pending.

Applicants acknowledge the allowance of claims 14-34.

Applicants have canceled claims 1-11 which are now present in a divisional application filed on January 7, 2005.

Applicants have also canceled claims 63, 65, 67 and 69 which will be presented in a continuation application along with the previously canceled claims 35-37, 54 and 55.

Applicants also hereby amend claims 12, 64 and 71 in order to put them in condition of allowance and give arguments in order to respond to the Examiner's observations and to support the allowability of claims 12, 13, 38-53, 56-62, 64, 66, 68 and 70-77.

DOUBLE PATENTING

Claims 1-10 Statutory Double Patenting Under 35 U.S.C. § 101

Cancellation of claims 1-10 renders this rejection moot. Matter subjected to statutory double patenting provision under 35 U.S.C. § 101 is no longer present in the present application.

Claims 38-53 and 56-62 Provisional Rejection (Obviousness-Type Double Patenting)

Applicants ask that the provisional rejection of claims 38-53 and 56-62 for obviousness-type double patenting over the copending application 10/469,037 ('037 application) be withdrawn because the subject matter of these claims does not overlap that of the '037 application.

In fact, it results from the involved claims that

- the compounds of claims 38-53 and 56-62 of the instant application are C5-epimerized products (i.e. they are formed by a mixture of chains in which 40%-60% of the uronic acid units in said chains are those of iduronic acid) and, hence, they are heparin-like compounds, while the compounds of claims 30-31 of the '037 application are non-epimerized products (i.e. they are formed by a mixture of chains in which all of the uronic acid units in said chains are those of glucuronic acid) and, hence, they are heparosan sulfate compounds, so that the two families of products have a different chemical structure;
- the compounds of claims 38-53 and 56-62 of instant application have a sulfation degree of from about 2.3 to about 2.9, while the compounds of claims 30-31 of the '037 application have a sulfation degree of from 3.2 to 4, so that not only there is no overlapping in the sulfation degrees of the two families of compounds but also the chemical characteristics of the two families of compounds render said families different in kind.

In view of the above arguments, the obviousness-type double patenting rejection of claims 38-53 and 56-62 is overcome.

Claims 4, 11-13 and 71-77 Provisional Rejection (Obviousness-Type Double Patenting)

Rejection of claims 4 and 11

Cancellation of claims 4 and 11 renders the provisional rejection of these claims over claims 1-10 of the '606 application moot.

Rejection of claims 12, 13 and 71-77

Claims 12 (as currently amended), 13 and 71-77 of parent application stand provisionally rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of the copending Application No. 10/240,606 ('606 application).

Applicants submit that instant claims 12,13 and 71-77 concern particularly favorable features of the invention which require the selection of features for more than one element of the method of claim 4.

In particular, claims 12 and 13 require the selection of conditions for the O-desulfation step (performed with a solution of dimethyl sulfoxide/methanol 9/1 (V/V) at 60°C for 3 hours) and conditions for the O-sulfation step (performed by reacting a tertiary amine or quaternary ammonium salt of the selectively O-desulfated product with a calculated amount of a sulphating agent at a temperature of 0-5°C for 0.5-3 hours) which would not be obvious in view of the subject matter of claims 1-10 of copending application Serial No. 10/240,606.

Claims 71-77 require the selection of conditions for the oversulfation step and the O-desulfation step. The claims in '606 also do not suggest these combined features to one skilled in the art and do not render these claims obvious.

Applicant respectfully ask that the rejection of claims 12, 13 and 71-77 for obviousness-type double patenting be withdrawn.

CLAIM REJECTIONS - 35 U.S.C. § 112

Cancellation of claims 63, 65, 67 and 69 renders the rejection of these claims under 35 U.S.C. § 112 moot.

Claims 66 and 70 Rejection ("Prevention of Thrombosis")

The rejection of claims 66 and 70 under 35 U.S.C. § 112 has been maintained because the arguments of applicants are deemed to be not persuasive. Applicants apologize for being not exhaustive in submitting their arguments, in particular those concerning the relationship between the biological parameters and the prevention of thrombosis in humans, as illustrated in the cited references, and the same relationship set forth in the instant specification.

The references cited by applicants in their previous response are not simple statements in the prior art but (in particular the Barrowcliffe et al. book and the Casu review) authoritative publications illustrating that the prevention of thrombosis is a consolidated indication of heparin and heparin-like glycosaminoglycans.

The compounds of claim 38 are new glycosaminoglycans having improved properties in respect of heparin because they exhibit anti-Xa and HCII activities at least of the same order as that of standard heparin, an anti-IIa (antithrombin) activity higher than that of standard heparin and a global anticoagulant activity (expressed as aPTT titre) lower than that of standard heparin (see paragraph [0170] of the specification as published, US 2002/0062019 A1).

Applicants respectfully submit that the whole, above-cited Barrowcliffe et al. book (T.W. Barrowcliffe, E.A. Johnson and D.P. Thomas, "Low Molecular Weight Heparin," 1992 John Wiley & Sons) is based on the measure and the study of the coagulation parameters (in particular the anti-Xa, anti-IIa and aPTT activities) of the low molecular weight heparin and on their impact on prevention and treatment of thrombosis in the clinical practice.

In the attached paper, consisting of the title pages, of the Contents' pages, of pages 135-138 and of pages 153-155 of the Barrowcliffe et al. book, the use of Low Molecular Weight Heparin (LMWH, in comparison with Unfractionated Heparin – UH) in the

prevention of thrombosis and the biochemical basis of such preventive or curative use are extensively illustrated.

At page 136, line 7, the Authors cite and comment the first study showing the capability of LMWH of preventing experimental venous thrombogenesis and observe that the activity, found as high as that of UF, was due to the AntiXa/AntiIIa ratio of 2 (see lines 14-17).

Pages 153-155 are the first ones (out of 23) of an Authors' review of the clinical studies of LMWH in prophylaxis of thrombosis. In particular, in the last paragraph of page 154, they point out that the units of activity were measured by an APTT assay and that the LMWH had an anti-Xa/APTT ratio of 4 (fifth sentence of the paragraph). The importance of a biochemical parameter (anti Xa activity) is outlined at page 155, lines 4-11 and that of another parameter, i.e. of the Anti-Xa/Anti-IIa ratio is also shown at page 156, lines 6-7. Other LMWH/UH comparison studies made in the field of the prevention of thrombosis are listed in the "Contents" of the book.

Not only in the submitted, representative pages but also throughout the Barrowcliffe et al. book a very close relationship between the biological parameters of UH and LMWH and the effect of these glycosaminoglycans on the prevention of thrombosis in animals and in humans is seen.

Applicants respectfully submit that the products of claim 38 are heparin-like glycosaminoglycans and that the results given in paragraph [0170] of the specification as published are consistent with the teachings of the Barrowcliffe et al. book which put the prevention of thrombosis by UH and LMWH in close relationship with the biochemical coagulation parameters of the two compounds. In particular, the data appearing in paragraph [0170], alone or combined with the results obtained on the final compounds of Examples 12,

13 and 17 in comparison with UH and LMWH, are highly predictable for the use of the claimed compounds in the prevention of thrombosis and duly support the subsequent statements given in paragraphs [0171] – [0186].

Thus, applicants respectfully ask that the rejection of claims 66 and 70 under 35 U.S.C. § 112 be withdrawn.

Claims 64 and 68 Rejection (Control of the Coagulation)

The rejection of claims 64 and 68 under 35 U.S.C. § 112 has been overcome by replacing the terms “controlling” and “control” by the terms “regulating” and “regulation” in claim 64.

Claims 71-77 Rejection (25 to 50% on weight)

The rejection of claims 71-77 under 35 U.S.C. § 112 has been overcome by replacing “on weight” by “by weight” in claim 71. Minor amendments, in particular the addition of “%” after “25” and the suppression of the article “the” render the claim clearer.

CONCLUSION

Claims 1-11, 63, 65, 67 and 69 are cancelled.

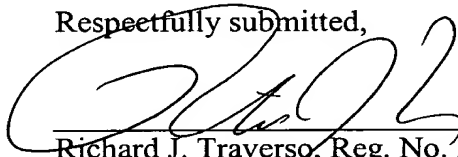
Claims 14-34 stand allowed.

The above amendments and arguments render claims 12, 13, 38-53, 64, 66, 68 and 70-77 allowable, which allowance is respectfully requested.

In view of the above, favorable reconsideration is courteously requested. If there are any remaining issues which can be expedited by a telephone conference, the examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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